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Erythropoietic Protoporphyria: A Case Report

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Abstract

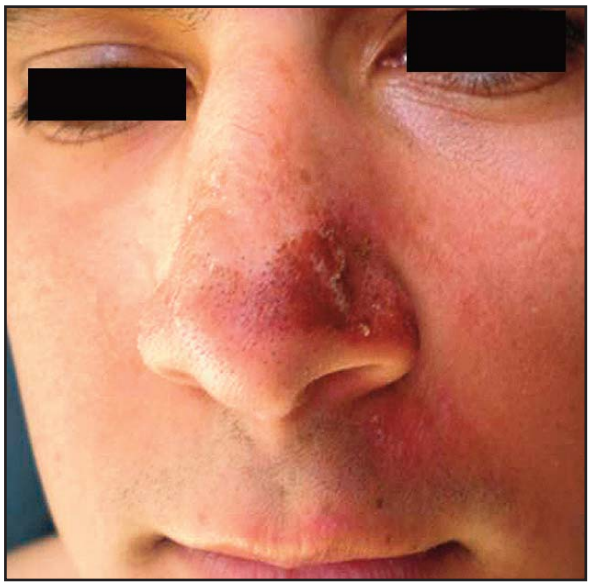
Observation: Erythropoietic protoporphyria (EPP) is an inherited disorder of haem biosynthesis, in which reduced activity of the enzyme ferrochelatase leading accumulation of protoporphyrins in various tissues. Protoporphyrins are photoactivated by ultra-violet light causing tissue damage by release of free oxygen radicals, which manifests as photosensitivity. EPP usually presents in early childhood or infancy with painful burning and pruritus within minutes of light exposure. Onset of symptoms in adults is rare and often associated with acquired somatic mutation of the FECH gene secondary to haematological malignancy. Herein we describe a 20-year-old male patient with EPP, who had a 15-year-history of recurrent swelling, blistering, itching, and burning on his nose, auricle and dorsa of hands after exposure to sunlight, which commenced in early spring of every year.

Introduction

Erythropoietic protoporphyria (EPP) is an inherited disorder of haem biosynthesis caused by decreased activity of the enzyme ferrochelatase (FECH), which catalyses the insertion of iron into protoporphyrin, the last step in haem biosynthesis. Development of clinically overt EPP usually requires inheritance of a severe FECH mutation trans to a low-expression FECH variant (FECH IVS3-48C) [1]. Reduced FECH activity leads to accumulation of protoporphyrin in various tissues. An excess amount of free protoporphyrin in the skin causes photosensitivity. EPP usually presents in early childhood or infancy, with severe burning pain of the skin with erythema, edema or bullae formation within minutes or hours of exposure to sunlight. Scars, pigmentation and depigmentation remain after the occurrence of acute skin lesions [2]. Herein we report a 20-year-old male patient with EPP with 15-year history of cutaneous complaints after exposure to sunlight who was diagnosed in adulthood.

Case Report

A 20-year-old man presented with a long history of pain, itching and burning sensation of the hands and face, together with a rash on his nose and auricle, following exposure to sunlight. The erythema, edema and blistering had been occurring immediately after sunlight exposure. His complaints which occur usually in spring and summer season, disappear spontaneously in the season of fall and winter. He had no family history with similar complaints and no consanguineous marriage between his parents.



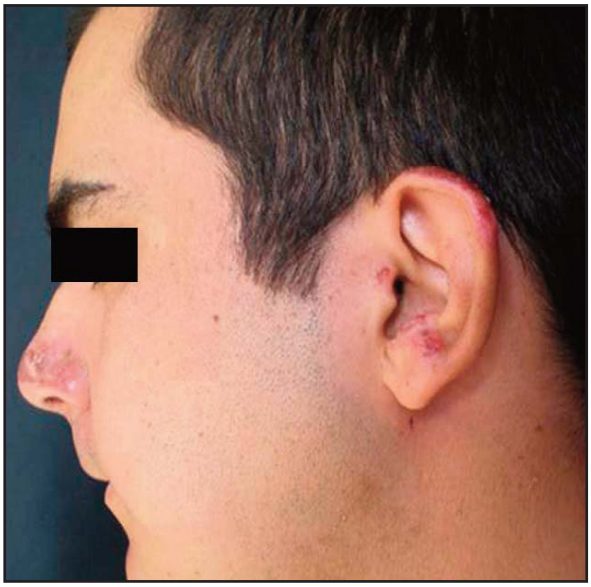


Figure 1 and 2. Erythematous, erosive, crusted rash on his nasal tip, nasal wing, upper lip, tragus, antitragus and helix of both auricle

On dermatological examination the patient demonstrated erythematous, erosive, crusted rash on his nasal tip, nasal wing, upper lip, tragus, antitragus and helix of both auricle (**Figures 1 and 2**). A few atrophic scars on the supranasal tip and auricle were noted. Complete blood count showed mild microcytic anemia with the 12.3 g/dl (normal range 13.6-17.2 g/dl) haemoglobin result. Routine biochemistry results including liver function tests, erythrocyte sedimentation rate, thyroid function tests, antinuclear antibody (ANA), anti-ds DNA antibody titres and urine porphyrin levels were within normal limits. Plasma and fecal total porphyrin levels and free erythrocyte protoporphyrin (FEP) levels were elevated.

Histopathology of a skin biopsy taken from nasal tip showed *Periodic-Acid–Schiff* (PAS) positive, amorphous eosinophilic deposits in the papillary dermis, especially surrounding the vessel walls and obliterating the vessel lumen. The diagnosis of EPP was confirmed with these results. Abdominal ultrasonography and liver function tests revealed no hepatic involvement. Although the eye complications of EPP had been reported in the literature, ophthalmologic examination didn't reveal any of them [**3**]. The patient was managed with topical antiseptics, epithelialising agents and broad spectrum sunscreens and sun avoidance. Annual physical examinations and laboratory studies were recommended, including FEP test, liver function tests, and complete blood count.

Discussion

In 1953, *Kosenow* and *Triebs* were the first to describe the clinical features of a cutaneous condition characterized by an immediate hypersensitivity to sunlight in a young boy with porphyrinemia. By 1961, their clinical description had been expanded upon and given the name erythopoietic protoporphyria by *Magnus* et al. In 1963, *Haeger-Aronsen* elucidated the genetic nature of EPP. Eventually in 1975, *Bottomly* et al reported the diminished activity of the enzyme ferrochelatase (FECH) in EPP [**2**].

Based on its etiology, erythropoietic protoporphyria is commonly classified as either a congenital autosomal dominant disease or as a disease of unknown cause. Hereditary EPP is due to an inherited deficiency of the ferrochelatase enzyme, which inserts the ferrous iron into the protoporphyrin ring to produce haem in the bone marrow and liver tissue. This deficiency results in both liver and bone marrow dysfunction due to the accumulation of the potent photosensitizer protoporphyrin, particularly in the red blood cells and internal organs [**4**]. The gene for ferrochelatase has been mapped to chromosome 18 (18q22) [**5**].

The patients with EPP complain with severe burning and pain of the skin with erythema, edema or bullae formation within minutes or hours of exposure to sunlight. Scars, pigmen-

tation and depigmentation remain after the occurrence of acute skin lesions. Porphyrins in the serum and red cells absorb 400 nm. ultraviolet light and radiate energy and also cause damage to the vessels, resulting with skin damage [**6**]. Patients normally present in early childhood. Onset in adulthood has rarely been reported, usually in association with myelodysplastic syndrome [**7**].

As protoporphyrin is strongly lipophilic, it is cleared by the liver and excreted in the bile. Cholelithiasis occurs with increased frequency and may occur at an early age in patients with EPP [**8**]. Massive deposition of protoporphyrin in liver parenchyma may lead to liver failure in 1–10% of patients [**9**].

Laboratory findings include high levels of free PP in red blood cells, plasma, and feces, but not in urine, due to the water insolubility of this porphyrin. While the urine porphyrin levels were within normal limits, free erythrocyte protoporphyrin [22 µmol/L, (normal <1.4 µmol/L)], plasma total porphyrin [50 nmol/L (normal <10 nmol/L)] and fecal total porphyrin levels [837 µmol/kg (normal <200 µmol/kg)] were elevated in our patient. These results were correlated with the laboratory findings of EPP.

In advanced hepatic failure, urinary coproporphyrin levels may be elevated because of impaired biliary excretion [**10**]. Some patients demonstrate a mild, microcytic anemia and abnormal serum transaminase levels [**2**].

Histopathology demonstrates extensive homogenous, amorphous eosinophilic deposits within and surrounding the thickened vessel walls of the superficial plexus. These deposits are composed of basement membrane material (collagen and laminin). They are PAS positive and diastase resistant, with a characteristic onion skin appearance. Also, hyalinization of the stroma in the papillary dermis is quite prominent [**11**].

Photoprotection with reflecting sunscreens containing zinc oxide or titanium dioxide, clothing, and beta-carotene administration is the mainstay of treatment in EPP. Palliative therapies such as cool compresses to the skin and antihistamines may reduce pruritus resulting from mast cell degranulation and histamine release during acute phototoxic reaction. Patient's education is important regarding the signs of liver dysfunction, such as abdominal pain, jaundice, icterus, and steatorrhea. In addition, patients should avoid hepatotoxic drugs such as ethanol, and cholestatic medications such as estrogen and anesthetics, which may slow down bile flow [**2**].

In conclusion, the diagnosis of EPP may be difficult. Patients might be misdiagnosed or haven't been diagnosed till their adulthood as in our patient. Erythrocyte and plasma protoporphyrin levels must be requested to assure a correct diagnosis from the patients with the history of photosensitivity and erosive rash on sun exposed areas. Patients will be able to managed and followed up for the vital complications as hepatic involvement with the correct diagnosis.

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